**DOCKET NO.: ISIS-5138 Application No.: 10/616,009** 

Office Action Dated: May 25, 2006

## REMARKS

In the Office Communication dated May 25, 2006, claims 1 and 29 to 74 were subject to restriction under 35 U.S.C. § 121 as follows:

- I. Claims 1, 29-44, 49, and 50, drawn to a mixed sequence antisense oligonucleotide comprising first and further portions, classified in class 536, subclass 24.5, for example.
- II. Claims 45 and 47, drawn to a mixed sequence antisense oligonucleotide comprising at least 8 nucleotides and having a 2'-OH arabinonucleotide sequence, classified in class 536, subclass 24.5, for example.
- III. Claims 46 and 48, drawn to a mixed sequence antisense oligonucleotide comprising at least 8 nucleotides and having a 2'-F arabinonucleotide sequence, classified in class 536, subclass 24.5, for example.
- IV. Claims 51-68, drawn to a method comprising contacting an oligonucleotide with RNA or DNA in vitro or in a cellular assay, classified in class 435, subclass 6, for example.
- V. Claims 69-71 and 74, drawn to a method for identifying and selecting an antisense oligonucleotide, classified in clas 435, subclass 6, for example.
- VI. Claims 72 and 73, drawn to an oligonucleotide for modulating a target nucleic acid identified using the process of claim 69, classified in class 536, subclass 24.5, for example.

It is stated in the Office Communication that the various groups are directed to unrelated subject matter. The examiner further stated that election of Group I requires a further election of a single species of 2' substituent for each of said first and further portions, respectively, recited in claims 33, 34, 36, and 37. The examiner stated that applicants must also elect a single species of linkage for said further portion, recited in claim 38.

Applicants respectfully traverse the restriction requirement. Applicants cancel claim 38 without prejudice to pursuing the claimed subject matter in a continuing application.

According to MPEP § 803, there are two criteria for a proper requirement for restriction between patentably distinct inventions:

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(A) The inventions must be independent (see MPEP § 802.01, § 806.04, § 808.01) or distinct as claimed (see MPEP § 806.05 to § 806.05(i)); and

(B) There must be a serious burden on the examiner if restriction is required (see MPEP § 803.02, § 806.04(a) to § 806.04(i), § 808.01(a), and § 808.02).

For purposes of the initial requirement, a serious burden may be *prima facie* shown if the examiner shows separate classification, separate status in the art, or a different field of search as defined in MPEP § 808.02. Groups I, II, III and VI are directed to oligonucleotides that are classified within the same class and subclass. The mixed sequence oligonucleotides of Groups I, II, and III and the oligonucleotides of group VI are capable of supporting cleavage of a complementary target RNA by human RNase H1 polypeptide. It would not be a serious burden on the examiner to search for different mixed sequence oligonucleotides of the same class and subclass, for example, class 536, subclass 24.5. Therefore as an initial matter, Groups I, II, III, and VI should be rejoined.

The compound and methods of the invention are related as product and process of use. Moreover, the examiner has failed to demonstrate any undue burden of conducting a search that would include claims of Groups I through VI. The oligonucleotide compounds of groups I, II, III and VI and the methods of Groups IV and V are related as products and method of use. Groups I, II, III and VI encompass oligonucleotides while groups IV and V are related to methods of using the oligonucleotides wherein the oligonucleotide modulates a target nucleic acid or the oligonucleotide supports cleavage of a complementary target RNA. A lack of serious burden exists because all of the claims of the instant application relate to a single concept of oligonucleotides capable of supporting cleavage of a complementary target RNA by human RNase H1 polypeptide. The oligonucleotides of Groups I, II, III and VI are useful in a method for contacting RNA or DNA in an *in vitro* assay or a cellular assay, or in a method of selecting an oligonucleotide for modulating the target in the presence of the human RNase H1 polypeptide in the cell. The mixed sequence oligonucleotides may have, for example, various ribonucleotide sequence components, 2'-OH arabinonucleotide sequence components, or 2'-F arabinonucleotide sequence components.

Contrary to the examiner's assertion, the compositions and the methods relate to the use of mixed sequence oligonucleotides. A common component of the claims in Groups I

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through VI are that a portion of the oligonucleotide is capable of supporting cleavage of a complementary target RNA by human RNase H1 polypeptide. Accordingly, applicants respectfully request rejoinder of the claims of Groups II, III, IV, V and VI with the claims of elected Group I in the present application.

Thus, applicants respectfully request the examiner to reconsider the restriction requirement, and in particular to consider it only a provisional election of species for the purpose of carrying out the search. Nonetheless, to be fully responsive to the restriction requirement, applicants elect with traverse to prosecute the claims of Group I, mixed sequence oligonucleotides of claims 1, 29-37, 39-44, 49, and 50, for examination on the merits in the present application. Further, applicants elect, with traverse, a species of claim 34 wherein said 2' substituent is 2'-deoxyribonucleotide for the first portion. Applicants elect, with traverse, a species wherein said 2' substituent is 2'-O-alkyl for the further portion. Applicants have canceled claim 38 without prejudice to pursuing the claimed subject matter in a continuing application. Therefore, applicants are not required to elect a single species of linkage for the further portion, as recited in claim 38. Claims 1, 29, 30, 31, 32, 34, 35, 36, 39, 40, 41, 42, 43, 44, 49 and 50 read on the elected species.

The examiner has required restriction between product and process claims. Where applicants elect claims directed to a product and the product claims are subsequently found allowable, the withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claims will be rejoined in accordance with the provisions of MPEP § 821.04.

In view of the above, applicants respectfully request that the restriction under 35 U.S.C. § 121 be reconsidered and examination of the application on the merits, on the basis, initially, of the elected species commence. Should the examiner consider the elected species allowable, consideration of the full generic scope of pending Claims 1, 29-44, 49, and 50 is respectfully requested.

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## **CONCLUSION**

Applicants hereby elect, with traverse, Group I consisting of claims 1, 29-37, 39-44, 49, and 50. Solely to advance prosecution and without prejudice to pursuing the claims in a continuing application, claim 38 is cancelled, and claims 45-48, 51-74 are withdrawn. Applicants reserve the right to pursue the subject matter of all non-elected claims in one or more related applications. Applicants respectfully request an early and favorable action.

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